

9. (New) The method of claim 8 wherein the biological event is mediated by the association of two or more molecules of the same cell surface receptor and the first and second non-peptidic moieties are the same.
10. (New) The method of claim 9 wherein the cell surface receptor is a receptor for a cytokine, growth factor or other hormone.
11. (New) The method of claim 10 wherein the cell surface receptor is a receptor for erythropoietin ("EPO"), granulocyte colony stimulating factor ("G-CSF"), thrombopoietin ("TPO"), growth hormone ("GH"), interleukin-2 ("IL-2"), interferon-alpha, interferon-beta, or a neurotropic factor.
12. (New) The method of claim 8 wherein the biological event is mediated by the association of molecules of two different cell surface receptors and the first and second moieties are different.
13. (New) The method of claim 8 wherein the first and second non-peptidic moieties bind to cytoplasmic portions of the cell surface receptors.
14. (New) The method of claim 8 wherein the first and second non-peptidic moieties bind to extracellular portions of the cell surface receptors.
15. (New) The method of claim 8 wherein the agent binds to the cell surface receptors with a  $K_d \leq 10^{-6}$  M.
16. (New) The method of claim 8 wherein the first and second non-peptidic moieties have a molecular weight less than 5 kD.
17. (New) The method of claim 8 wherein the agent is membrane permeant.

18. (New) The method of claim 8 wherein the cell surface receptors are selected from the group consisting of epidermal growth factor-receptor (EGF-R), ataxia telangiectasia and rad-related 2/neuroblastoma oncogene (ATR2/neu), hermaphrodite homolog-2/neuroblastoma oncogene (HER2/neu), hermaphrodite-3/cellular-erythroblastic leukemia oncogene homolog-3 (HER3/c-erbB-3), Xiphophorus melanoma receptor tyrosine kinase homolog (Xmrk); insulin-like growth factor-I-receptor (IGF-1-R), insulin receptor-related receptor (IRR); platelet-derived growth factor receptor- $\alpha$  (PDGF-R- $\alpha$ ), platelet-derived growth factor receptor- $\beta$  (PDGF-R- $\beta$ ), colony stimulating factor-1-receptor (CSF-1-R, macrophage-colony stimulating factor-receptor (M-CSF-R)/cellular-McDonough feline sarcoma homolog (c-Fms)), c-kit (Steel Factor Receptor, mast/stem cell growth factor receptor, HZ4-feline sarcoma virus viral oncogene homolog), serine/threonine kinase/fms-like tyrosine kinase 2 (STK-1/Flk-2); fibroblast growth factor-receptor FGF-R (FGF-R), [acidic-] fibroblast growth factor-receptor-1 (flg), [basic-] fibroblast growth factor-receptor-2 (bek); neurotrophic tryosine kinases; cell-surface determinant-3-z (CD3-z) and cell surface/class II determinant-3-e (CD3-e);  $\beta$  and g chains of Fc/IgE receptor-1 (FCERI); g chain of Fc receptor/cell-surface determinant-16 (Fc $\gamma$ -RIII/CD16); cell-surface determinant-3-g, -d and -e subunits (CD3-g, -d and -e); Ig- $\alpha$  subunit of B-cell antigen receptor complex/membrane-bound, Ig-associated protein-1 (Ig- $\alpha$ /MB-1) and Ig- $\beta$  subunit of B-cell antigen receptor complex/c membrane-bound, Ig-associated glycoprotein B29 (Ig- $\beta$  /B29); the common  $\beta$  subunit shared by the granulocyte/macrophage-colony stimulating factor (GM-CSF), interleukin-3 (IL-3) and interleukin-5 (IL-5) receptors; the  $\beta$  chain of glycoprotein MW 130 KD (gp130) associated with the interleukin-6 (IL-6), leukemia inhibitory factor (LIF), ciliary neurotrophic factor (CNTF), oncostatin M, and interleukin-11 (IL-11) receptors; the interleukin-2 (IL-2) receptor gamma subunit associated also with receptors for interleukin-4 (IL-4), interleukin-7 (IL-7) and interleukin-13 (IL-13); the  $\beta$  chain of the interleukin-2 (IL-2) receptor; receptors for interferons (IFN)  $\alpha/\beta$  and  $\gamma$ ; receptors for growth hormone (GH), erythropoietin (EPO) and prolactin; and the Transforming growth factor- $\beta$  (TGF- $\beta$ ) family of cell surface receptors.

19. (New) A method for preparing an agent that effects a biological event mediated by the association of two or more endogenous protein mediators, the method comprising preparing an agent which includes a first non-peptidic moiety that binds to one of the protein mediators

covalently linked with a second non-peptidic moiety that binds to the other protein mediator, wherein the agent binds to both protein mediators, the biological event is mediated by the association of molecules of two different protein mediators and the first and second moieties are different.

20. (New) The method of claim 19 wherein at least one of the protein mediators is a cell surface receptor.

21. (New) The method of claim 19 wherein the two different protein mediators are cell surface receptors.

22. (New) The method of claim 19 wherein the biological event is transcriptional regulation, the first non-peptidic moiety binds to a protein containing a DNA-binding domain and the second non-peptidic moiety binds to a protein containing a transcriptional regulatory domain.

23. (New) The method of claim 22 wherein the transcriptional regulatory domain is a transcriptional activation domain.

24. (New) The method of claim 22 wherein the transcriptional regulatory domain is a transcriptional repression domain.

25. (New) The method of claim 19 wherein the biological event is translocation of a selected protein to a predetermined cellular component, the first non-peptidic moiety binds to the selected protein and the second non-peptidic moiety binds to a constituent of the predetermined cellular compartment.

26. (New) The method of claim 25 wherein the first non-peptidic moiety binds to a protein that functions only in the cytoplasm and the second non-peptidic moiety binds to a constituent of the nucleus or mitochondrion.

27. (New) The method of claim 19 wherein the biological event is destruction of a selected protein, the first non-peptidic moiety binds to the selected protein and the second non-peptidic moiety binds to a constituent of the proteasome.

28. (New) The method of claim 8 or 19 further comprising mixing the agent with a pharmaceutically acceptable carrier and optionally with one or more pharmaceutically acceptable excipients.

29. (New) A method which comprises providing an agent prepared according to the method of claim 8 or 19 and mixing the agent with a pharmaceutically acceptable carrier and optionally with one or more pharmaceutically acceptable excipients.

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### Remarks

#### Amendment

Claims 1-7 are pending and stand rejected. The present Amendment cancels claims 1-7.

The present Amendment also adds new claims 8-29. Claims 9-18 are dependent claims that depend from independent claim 8. Claims 20-27 are dependent claims that depend from independent claim 19. Claims 28 and 29 are multiple dependent claims that depend from either one of claim 8 or 19.

New claims 8 and 19 have been derived from canceled claim 1. Both claims specify that the inventive agent includes first and second moieties that are *non-peptidic* (e.g., as recited in canceled claim 7). Claim 8 further specifies that the inventive agent binds to protein mediators that are *cell surface receptors* (e.g., as recited in canceled claim 3 and also page 3, line 27 - page 4, line 9; page 4, lines 19-23; page 5, lines 17-20; page 7, line 22 - page 10, line 23). Claim 19 further specifies that the first and second moieties are *different* and that the inventive agent binds to two *different* protein mediators (e.g., as recited in canceled claim 5 and also page 5, lines 21-23; page 12, line 22 - page 13, line 2).

New dependent claims 9-18 and 20-29 are also supported by the application as filed, e.g., as follows: